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09/485,601 05/04/00 STRITTMATTER

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HM12/0703

EXAMINER

KERR, K

ART UNIT

PAPER NUMBER

1652

DATE MAILED:

07/03/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trad marks

Office Action Summary

Application No.
09/485,601

Applicant(s)
Strittmatter

Examiner
Kathleen Kerr

Art Unit
1652



-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 4/23/01
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1, 2, 6-13, 17, and 21-30 is/are pending in the application.
- 4a) Of the above, claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 2, 6-13, 17, and 21-30 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- 11) ☒ The proposed drawing correction filed on 4/23/01 is: a) ☐ approved b) ☒ disapproved.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

- 13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- a) ☐ All b) ☐ Some* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

- 14) ☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

- 15) ☐ Notice of References Cited (PTO-892) 18) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 16) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948) 19) ☐ Notice of Informal Patent Application (PTO-152)
- 17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____ 20) ☐ Other: _____

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DETAILED ACTION

Application Status

1. In response to the first Office action on the merits (Paper No. 9 mailed on January 17, 2001), Applicants filed a response on April 23, 2001 (Paper No. 10). Said response amended the specification and claims 1, 6, 8, 12, and 17, canceled claims 3-5, 14-16, and 18-20, and added new claims 21-30. The Examiner notes that amendments to Claims 12 and 17 converted said claims into method claims from their original product claims.

Claims 1, 2, 6-13, 17, and 21-30 are pending in the instant application and will be examined herein.

Priority

2. As previously noted, Applicant is granted the benefit of priority for the provisional application 60/055,268 filed on August 13, 1997 and the internationally filed application PCT/US98/16794 filed on August 12, 1998 as requested in the declaration.

Also as previously noted, the subject matter of Claims 8 and 17 was not disclosed in the provisional application and, thus, is granted a priority date of August 12, 1998 for the international filing. The subject matter of all other claims was disclosed in the provisional application and, thus, is granted a priority date of August 13, 1997 for the provisional application.

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Drawings

3. Previously, the drawings were considered informal. Applicants' response to the previous Office action included the filing of new drawings. Said new drawing are also considered informal for the reasons detailed in the attached copy of PTO Form 948. Appropriate correction is required prior to allowance.

Withdrawn - Objections to the Specification

4. Previous objection to the title for not being adequately descriptive of the claimed subject matter is withdrawn by virtue of Applicants' amendment.
5. Previous objection to the specification for lacking an abstract of the disclosure is withdrawn by virtue of Applicants' amendment.
6. Previous objection to the specification for lacking specificity on page 13, lines 20-28, which discloses particular amino acid residues of a protein, rho, is withdrawn by virtue of the Examiner's reconsideration in view of Applicants' arguments.
7. Previous objection to the specification for the use of undefined abbreviations is withdrawn by virtue of Applicants' amendment to the specification.

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Withdrawn - Objections to the Claims

8. Previous objection of Claims 1, 2, 6-11 for containing non-elected subject matter is withdrawn by virtue of Applicants' amendment to the instant claims.
9. Previous objection to Claim 6 under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim, is withdrawn by virtue of Applicants' amendment to the instant claim.

Withdrawn - Claim Rejections - 35 U.S.C. § 112

10. Previous rejection of Claims 1, 2, and 6-11 under 35 U.S.C. 112, first paragraph, enablement, is withdrawn to the extent that said rejection was a full scope of enablement rejection. Applicants' arguments have been fully considered, and the Examiner has reconsidered the rejection.

Applicants argue that DRG neurons are both central and peripheral, contrary to the Examiner's statement that DRG neurons are not indicative of central neurons, referencing Vastrik et al. and Lehmann et al. The Examiner finds no clear support for this statement in either reference, unlike the support cited in the Examiner's rejection as found in Jackowski. The Examiner maintains the previous reasoning that examples presented in the instant application using DRG neurons are NOT indicative of CNS neurons. However, Lehmann et al. (a reference post-dating the filing date of the instant application) do convincingly demonstrate, using optic (central) nerves of rats, that Applicants' claims to methods for promoting CNS axon growth using

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C3 toxin are effectively enabled. Thus, it appears that Applicants' claims, although not clearly enabled by the instant specification, are effective and productive and, thus, enabled, to the extent that an active portion of C3 toxin is administered.

Withdrawn - Claim Rejections - 35 U.S.C. § 102

11. Previous rejection of Claim 12 under 35 U.S.C. 102(b) as being anticipated by Morii et al. is withdrawn by virtue of Applicants' amendment changing Claim 12 from a product claim into a method claim, which method claim is not anticipated by Morii et al.

Withdrawn - Claim Rejections - 35 U.S.C. § 103

12. Previous rejection of Claim 17 under 35 U.S.C. 103(a) as being unpatentable over Barth et al. in view of Morii et al. is withdrawn in view of Applicants' amendment changing Claim 17 from a product claim into a method claim, which method claim is not obviated by the combination of Barth et al. and Morii et al.

Maintained - Claim Rejections - 35 U.S.C. § 112

13. Previous rejection of Claims 1, 2, 6, and 9-12 under 35 U.S.C. 112, second paragraph, as being indefinite for the term "rho protein inhibitor" is maintained. As previously noted, in the instant specification, rho inhibitors are described as many things (see instant specification, page 10) including inhibitors of rac, cdc42, or other proteins in the GTP-binding family. The inclusion

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of the phrase “in amounts effective to inhibit rho or rac” only serves to further confuse the term; are only rho and rac inhibitors included in the metes and bounds of the claim or are all the GTP-binding family members, such as found in the instant specification on page 10, included?

Applicants present no arguments traversing the rejection; Applicants amended Claim 1, which amendment does not clarify the claim as noted above. Appropriate definition of the metes and bounds of the instant claim, particularly of the term “rho protein inhibitor”, is required.

14. Previous rejection of Claims 8 and 17 under 35 U.S.C. 112, second paragraph, as being indefinite for the term C2/C3 inhibitor is maintained. As previously noted, the structure of a C2/C3 chimeric *C. botulinum* construct is not clear. Applicants' amendment inserts required activities of the chimeric protein, not required structure.

Applicants present no arguments traversing the rejection; Applicants amended Claim 8, which amendment does not clarify the claim as noted above. Appropriate definition of the metes and bounds of the instant claim, particularly of the C2/C3 construct, is required.

15. Previous rejection of Claims 1, 2, 6, and 8-11 under 35 U.S.C. 112, first paragraph, enablement, is maintained. The Examiner notes that the initial rejection was a lack of enablement for the full scope of the claims which included reasoning for (1) the full scope rejection as well as (2) a partial scope rejection; the maintained rejection is herein amended to be a partial scope of enablement rejection only as reiterated below. (See also above concerning the withdrawal of the full scope of enablement rejection.)

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Claims 1, 2, 6, and 8-11 are rejected under 35 U.S.C. 112, first paragraph, scope of enablement, because the specification, while being enabling for methods of axon regeneration using C3 exoenzyme, does not reasonably provide enablement for methods of axon regeneration using *any* rho protein inhibitor. The Examiner notes that Claim 8 is included in the instant rejection in view of the 112, second paragraph, rejection above concerning the clarity of the C2/C3 construct. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims. This rejection is the same rejection previously presented and reiterated below from Paper No. 9, item 14, the first issue presented, scope of enablement.

“[T]he instant specification provides a single example of a rho protein inhibitor for use in the claimed methods, the C3 exoenzyme from *C. botulinum*. While experimentation to determine other inhibitors of rho protein is not without direction, the instant specification provides no suggestion that administration of any other rho protein inhibitor will promote CNS axon growth. The state of the art is such that nerve growth and/or regeneration is a complex process in which “multiple inhibitory proteins exist, and, for efficient axon regeneration in adult CNS, it will be important to neutralize their inhibitory effects” (see Lehmann et al. IDS, page 7537, first paragraph). Thus, the unpredictability in using other rho protein inhibitors limits the scope of the claims which may be enabled by the instant specification. This same argument extends to the use of an undefined chimera of C2/C3 exoenzyme since Applicant’s examples are directed at the full-length C3 exoenzyme and the C2/C3 exoenzyme chimera need not contain the entire C3 exoenzyme.”

Applicants’ arguments traversing the instant rejection are based on the similarity of “rho protein inhibitors”. As noted below in the Examiner’s response to Applicants’ traversal of the written description rejection, a single example in such a broad genus does not enable the entire genus for

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the instant methods. The Examiner's rejection, as reiterated above, clearly set forth this point which is herein maintained.

16. Previous rejection of Claims 1-2, 6, and 9-12 under 35 U.S.C. 112, first paragraph, written description, is maintained. The instant claims are drawn to methods of using rho protein inhibitors and, the Examiner maintains, Applicants have not described a representative number of species in such a large genus. Applicants' arguments have been fully considered but are not considered persuasive for the following reasons.

Applicants argue that, upon the availability of the human genome, all the GTP-binding proteins are now identified. The Examiner disagrees with this generalization. While the human genome may be fully sequenced, the functionality of all its possible genes has not nearly been completely analyzed. Moreover, no limitation of human rho protein inhibitors is included in the instant claims so that availability of the *human* genome is not wholly applicable. The Examiner has noted Nobes et al., as supplied by Applicants, and has failed to identify any evidence in Nobes et al. to convince the Examiner that the disclosure of a single rho protein inhibitor effectively describes the broad genus. For all of the above reasons, the instant rejection is maintained.

Maintained - Claim Rejections - 35 U.S.C. § 102

17. Previous rejection of Claim 13 under 35 U.S.C. 102(b) as being anticipated by Morii et al. is maintained. Applicants' response describes an amendment to Claim 13; however, no such

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amendment is set forth. Applicants present no other arguments. The instant rejection is, therefore, maintained.

NEW REJECTIONS

Claim Rejections - 35 U.S.C. § 112

The following are continuations of above rejections newly applied to newly added or amended claims.

18. Claims 21-23 and 25-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for the term “rho protein inhibitor” as set forth above and in a previous Office action for Claims 1, 2, 6, and 9-12.

19. Claim 30 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for the term C2/C3 inhibitor as set forth above and in a previous Office action for Claims 8 and 17.

20. Claims 12, 17, 21-23, 25-28, and 30 are rejected under 35 U.S.C. 112, first paragraph, scope of enablement, because the specification, while being enabling for methods of axon regeneration using C3 exoenzyme, does not reasonably provide enablement for methods of axon regeneration using *any* rho protein inhibitor as set forth above and in a previous Office action for Claims 1, 2, 6, and 8-11. The Examiner notes that Claims 12, 17, 23, 28, and 30 are included in

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the instant rejection in view of the 112, second paragraph, rejection above concerning the clarity of the C2/C3 construct and the clarity of "a *C. botulinum* C3 inhibitor".

21. Claims 21-22 and 25-27 are rejected under 35 U.S.C. 112, first paragraph, written description, as set forth above and in a previous Office action for Claims 1-2, 6, and 9-12.

The following are newly developed rejections necessitated by Applicants' amendments.

22. Claims 8 and 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 24 depends from itself and, thus, is wholly unclear; Claim 8 is unclear by virtue of its dependency on Claim 24 without correcting the defect. Appropriate clarification is required.

23. Claims 12, 13, and 25-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In Claim 12, it is unclear how a rho protein can be an inhibitor of itself. Appropriate clarification is required.

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24. Claims 23 and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term “a *C. botulinum* C3 inhibitor” is confusing because throughout the instant specification and the claims, the *C. botulinum* C3 protein is called an exoenzyme. Moreover, the article “a” indicates that the claims encompass *any* C3 protein; however, the metes and bounds of such a genus are undefined in the instant specification. Appropriate clarification is required.

25. Claim 30 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In line 1, the term “the composition” has no antecedent basis. Appropriate correction is required.

Summary of Pending Rejections

26. The following is a summary of the pending rejections of the instant claims.
- a. Claims 1, 2, 6, 9-12, 21-23, and 25-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for the term “rho protein inhibitor”
 - b. Claims 8, 17, and 30 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for the term C2/C3 inhibitor.

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- c. Claims 1, 2, 6, 8-11, 12, 17, 21-23, 25-28, and 30 are rejected under 35 U.S.C. 112, first paragraph, scope of enablement.
- d. Claims 1-2, 6, 9-12, 21-22, and 25-27 are rejected under 35 U.S.C. 112, first paragraph, written description.
- e. Claim 13 is rejected under 35 U.S.C. 102(b) as being anticipated by Morii et al.
- f. Claims 8 and 24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite because Claim 24 depends from itself.
- g. Claims 12, 13, and 25-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite because it is unclear how a rho protein can be an inhibitor of itself.
- h. Claims 23 and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for the term “a *C. botulinum* C3 inhibitor”.
- i. Claim 30 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite because the term “the composition” has no antecedent basis.

Conclusion

27. No claims are allowed in the instant application for the reasons identified in the numbered sections of this Office action. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

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Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

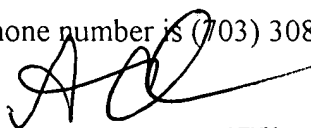
Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Dr. Kathleen M. Kerr whose telephone number is (703) 305-1229. The Examiner can normally be reached on Monday to Friday from 8:30 a.m. to 5:00 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. Ponnathapura Achutamurthy, can be reached on (703) 308-3804.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

KMK

July 1, 2001


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